REMARKS

I. Claim Status

Claims 3-8 are currently pending and stand rejected. Claim 3 has been amended herein. That claim is supported in, at least, original claim 3. Accordingly, no new matter is added.

II. Enablement Rejection

The Examiner rejected claim 3 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. Final Office Action dated January 15, 2009 ("Final Office Action") at 2. Applicants respectfully traverse this rejection.

The Examiner has failed to establish a *prima facie* case of nonenablement. There is a strong presumption that a specification, having a disclosure "which contains a teaching of the manner and process of making and using an invention" complies with the enablement requirement "unless there is a reason to doubt the objective truth of the statements" in the specification. *See* M.P.E.P. § 2164.04 (citing *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). Because the present specification teaches an exemplary method for making and using the presently claimed invention that reasonably relates to the scope of claim 3, the enablement requirement is met. In other words, one of ordinary skill in the art would have been able to practice the claimed invention without undue experimentation.

In particular, the specification discloses an exemplary method for making dosage forms "suitable for the treatment of renal failure." *See* Specification, p. 4, lines 27-36 and p 5, lines 1-27. In addition, the specification discloses exemplary doses and administration routes for practicing the claimed invention. *See id*, p. 4, lines 13-25 and

p. 5, lines 29-32. Even without more, this disclosure is sufficient to overcome the rejection.

However, the specification also provides a working example of practicing the claimed invention. The example on pages 6-7 demonstrates that the mortality in patients with renal impairment was reduced to a greater extent than those patients with normal renal function upon treatment with levosimendan. Specifically, mortality in patients with renal impairment was reduced by 49% from the control group, whereas the mortality in normal renal patients was reduced by only 37% over the control group.

In other words, levosimendan lowered mortality across the board for patients receiving the drug (col. 2 of the table), but the difference between the two levosimendan groups was that one included normal renal patients and one included patients with impaired renal function. In the latter group, if levosimendan were only affecting the mortality associated with cardiovascular problems as it did in the group with normal renal patients (col. 2, row 2), then the reduction in mortality of the renally impaired group would be expected to be the same as that for the normal patient group (col. 2, row 3). However, as pointed out, there was an additional 12% lowering in mortality in patients with renal impairment. That 12% difference between the normal and renally-compromised patients is attributed to "the beneficial effects of levosimendan on impaired renal function." Specification, p. 7, line 19.

Lower mortality as a result of levosimendan's beneficial effects on kidney function necessarily means that kidney function was improved or "treated." Thus, the disclosed example provides a concrete reduction to practice of the claimed invention

(claim 3). For this additional reason, the specification complies with the enablement experiment, and this rejection should be withdrawn.

III. Obviousness Rejection

The Examiner rejected claims 4-8 under 35 U.S.C. § 103(a) as allegedly obvious over Pagel, P. S., et al. "Pharmacology of Levosimendan: A New Myofilament Calcium Sensitizer," *Cardiovascular Drug Reviews* (1996) 14(3):286-316 ("Pagel") in view of Al-Ahmad, A., et al. "Cause and Management of Heart Failure Patients With Chronic Renal Disease," *Seminars in Nephrology* (2001) 21:3-12 ("Al-Ahmad"). Applicants respectfully traverse this rejection.

For the purposes of responding to the present rejection, Applicants will make reference to both Pagel and Sandell, E. P., et al. "The Effects of Renal Failure on the Pharmacokinetics of Levosimendan," *Therapie* (Suppl 1) (1995) 50:S495 ("Sandell"), submitted with Applicants' October 1, 2008, Response. Sandell relates to the underlying work discussed in Pagel at page 304.

In Applicants' last response dated October 1, 2008, Applicants argued that Pagel and Sandell do not expressly or inherently anticipate the presently pending claims. Consequently, the Examiner withdrew the § 102 rejection over Sandell.

Because neither Sandell nor Pagel expressly or inherently anticipate the present claims, the presently pending claims are likewise not obvious over either Pagel or Sandell. As the M.P.E.P. points out "[o]bviousness cannot be predicated on what is not known at the time an invention was made, even if the inherency of a certain feature is later established." M.P.E.P. § 2141.02.V. Properties that "may be inherent [are] not necessarily known. Obviousness cannot be predicated on what is unknown." *In re*

Shetty, 566 F.2d 81, 86, 195 U.S.P.Q. 753, 757, (C.C.P.A. 1977), quoting *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966). Following this Federal Circuit precedence, no *prima facie* case of obviousness over Pagel or Sandell can be made.

Moreover Al-Ahmad does not compensate for the deficiencies of Pagel and Sandell, and the pending claims are likewise not obvious over the presently cited combination of documents. Indeed, Al-Ahmad and Pagel actually teach away from each other, and as a result their teachings cannot be combined. *See* M.P.E.P. § 2145 (X)(D)(2). For example, Al-Ahmad discloses several currently employed drugs for treating patients who have both congestive heart failure and renal failure. *See* Al-Ahmad at 8-10. Those drugs include many of the very same drugs that Pagel discloses as not being ideal for the treatment of congestive heart failure. *See* Pagel at 286.

And, Al-Ahmad (2001), which published ***after*** Pagel (1996), does not even contemplate levosimendan among the potential therapeutic possibilities (pp. 8-10) to manage the health of patients with both heart failure and chronic renal disease. Such an omission would suggest to one of ordinary skill in the art that Al-Ahmad was aware of levosimendan's hypotensive effects, which can be dangerous in renal failure patients, even though levosimendan had been shown to be an effective treatment for heart failure. In fact, even after the filing date of the present application, health authorities continue to warn doctors and patients that "Levosimendan should not be used in patients with . . . severe kidney or liver impairment . . . ." News Release dated November 16, 2005 (submitted herewith in an Information Disclosure Statement). Consequently, Al-Ahmad's clear omission of levosimendan from its list of potential

drugs does the opposite of rendering the present claims obvious—it actually suggests that there would have been little expectation of success of using levosimendan for the treatment of renal failure (claim 3) or lowering mortality "associated with the deterioration of kidney function" (claim 4). Rather, one of ordinary skill in the art, based on Al-Ahmad's teachings would have been led away from administering levosimendan to a patient with renal failure.

For the reasons discussed above, this rejection should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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